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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,257	BENDER ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-17 and 19-37* is/are pending in the application.

4a) Of the above claim(s) *12,13,16,17,21,22,26-30 and 34-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11,14,15,19,20,23-25 and 31-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/13/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 5, 7 to 17 and 19 to 37 are pending in the instant application. Claim 14 has been amended as requested by Applicant in the correspondence filed 09 June of 2004.

2) Claims 12, 13 16, 17, 21, 22, 26 to 30 and 34 to 37, as well as claim 33 in so far as it depends from claim 7, are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3) The instant specification does not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 1A of the instant application, for example, is presented on two separate panels. The two sheets of drawings which are labeled " Figure 1A" in the instant specification should be renumbered "Figures 1A and 1B". The remaining figures should be renumbered accordingly. It is also noted that the specification refers to the drawings by employing lower case letters, which is incorrect. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

4) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no sequence listing has been provided which includes the nucleotide sequence identified as "d5HT 4B" in Figure 1A and the amino acid sequence identified as "d5HT 4B" in Figure 1B of the instant application. Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification **and abstract** will also need to be amended so that they comply with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

5) Claims 1, 7 and 14 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 is improper because it depends from itself. Claims 7 and 14 are improperly dependant

because they can be infringed by a polypeptide composition that does not infringe claim 1. A properly dependent claim can not conceivably be infringed without infringing any of the claims from which it depends. See M.P.E.P. 608.01(n)III.

6) Claim 33 is objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> "Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Harnish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

An antibody of claim 30 an a nucleic acid molecule of claim 1 do not share a common utility that is based upon a common structural feature. In fact, these two compounds are functionally, structurally and chemically unrelated.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7) Claims 1 to 4, 7 to 11, 14, 15, 19, 20, 23 to 25 and 31 to 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention and in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In so far as these claims encompass an isolated nucleic acid molecule encoding a "human 5-$HT_{4(h)}$ receptor" having other than the amino acid sequence presented in SEQ ID NO:2 of the instant application, no such receptor is described. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a single isolated cDNA encoding a particular, naturally occurring human receptor protein having very specific physical and structural properties, the instant specification does not provide a structural formula which is definitive of a genus of nucleic acids or proteins. Whereas the instant specification may identify some properties which are common to the 5HT receptors that are disclosed in the instant specification and the prior art, it does not identify those defining structural elements which provide the functional and structural properties of that genus of proteins that might be encompassed by the limitation "human 5-$HT_{4(h)}$ receptor". *In re Clarke*, 148 USPQ 665, (CCPA 1966) held that;

> " It appears to be well settled that a single species can rarely, if ever, afford support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.21 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of a small genus such as halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary."

One of ordinary skill in the art of receptor biology would not regard the disclosure of a single, naturally occurring, human protein as a representative number species of the genus of proteins potentially encompassed by the term "human 5-$HT_{4(h)}$ receptor".

In so far as the instant claims encompass a nucleic acid encoding a "functional equivalent" or "derivative" of a ""human 5-$HT_{4(h)}$ receptor", or the protein encoded

thereby, the instant specification does not provide the guidance that is needed to alter the amino acid sequence of SEQ ID NO:2 in a predictable manner. Specifically, the instant specification does not identify those amino acid residues in the amino acid sequence of SEQ ID NO:2 which are essential for the biological activity and structural integrity of "human 5-$HT_{4(h)}$ receptor" and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 400 amino acid residues before they could even begin to rationally design a functional 5-$HT_{4(h)}$ receptor having other than a natural amino acid sequence. The disclosure of a single DNA sequence encoding a single "human 5-$HT_{4(h)}$ receptor" with a natural amino acid sequence is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass any and all functionally equivalent proteins, including "derivatives" thereof, which are encoded by a DNA which hybridizes to a DNA having that single disclosed sequence "under conditions of high stringency".

The current claim limitations are directly analogous to those of claim 7 of U.S. Patent Number 4,703,008 which were held to be invalid under 35 U.S.C. 112, first paragraph, for want of enablement in *Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd.*, 18 U.S.P.Q. 2d, 1016 (CAFC, 3/5/91, see page 1026, section D). In that instance, a claim to a nucleic acid encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. § 112, first

paragraph, for want of enablement. This limitation is directly analogous to the hybridization limitation of the instant claims. The disclosure upon which that claim was based described a recombinant DNA encoding EPO and a few analogs thereof. That disclosure differs from the instant specification because, whereas the instant specification describes a DNA encoding a single "human 5-$HT_{4(h)}$ receptor", it does not describe even a single variant thereof. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For DNA sequences, that means disclosing how to make and use enough sequences to justify the grant of the claims sought. As indicated, the instant specification is even more limited than the '008 patent because it describes only a single protein and no analogs or mutants thereof and, therefore, provides even less support than the '008 specification for claims of comparable scope and which were held to be invalid in that patent.

Further, *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that :

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their

performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Whereas one could readily incorporate modifications into the amino acid sequence presented in SEQ ID NO:2 of the instant application, one can not reasonably predict the effects of those modifications by following the guidance provided by the instant specification and the prior art of record. The instant specification discloses that a "human 5-$HT_{4(h)}$ receptor" of the instant invention has a specific and substantial utility in the identification of potentially useful therapeutics. This utility, however, is only applicable to a receptor protein that produces a response that is predictive of an authentic, *in vivo* response. Because an artisan of receptor biology can not modify the amino acid sequence of SEQ ID NO:2 and "predicted by resort to known scientific law" if the modified receptor retains the ability of producing an authentic response, and the instant specification does not disclose how to use a receptor protein that does not produce an authentic response, the guidance provided by the instant specification is not commensurate with the scope of the instant claims.

Additionally, the instant specification does not disclose how to use a pharmaceutical composition comprising an isolated nucleic acid molecule as claimed in claim 20. There is not a single instance described in either the instant specification or the art of record of the successful administration of a nucleic acid encoding a G protein-coupled receptor or a nucleic acid antisense thereto to a mammal for clinical effect. A patent is granted for a completed invention, not the general suggestion of an idea and

how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not following the guidance presented therein and use the claimed pharmaceutical composition without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8) Claims 1 to 5, 7 to 11, 14, 15, 19, 20, 23 to 25 and 31 to 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8.1) Claims 1 to 5, 7 to 11, 14, 15, 19, 20, 23 to 25 and 31 to 33 are vague and indefinite in so far as they employ the term "human 5-$HT_{4(h)}$ receptor" as a limitation. Because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a "human 5-$HT_{4(h)}$ receptor" an

artisan can not determine if a compound which meets all of the other limitations of a claim would then be included or excluded from the claimed subject matter by the presence of this limitation. It is unclear how a claim to "an isolated serotonin receptor comprising the amino acid sequence of SEQ ID NO:2" would differ from a claim to "an isolated human 5-$HT_{4(h)}$ receptor comprising the amino acid sequence of SEQ ID NO:2".

8.2) Claim 1 is vague and indefinite because it depends from itself. Claims 2 to 5, 7 to 11, 14, 15, 20 and 31 to 33 are vague and indefinite in so far as they depend from claim 1 for this element.

8.3) Claim 1 is vague and indefinite because the limitation "conditions of high stringency" is conditional and no single set of defining conditions has been provided by the art of record or the instant specification. Those conditions described on page 8 of the instant specification are expressly identified therein as being exemplary. Claims 2 to 5, 7 to 11, 14, 15, 20 and 31 to 33 are vague and indefinite in so far as they depend from claim 1 for this element.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9) Claims 7 and 14 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims encompass a human protein as it occurs in nature.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10) Claims 1 to 4, 7 to 11 14, 15, 19, 20, 23 to 25 and 31 to 33 are rejected under 35 U.S.C. 102(b) as being anticipated by the Synaptic patent publication (WO 94/14957, 07 July 1994, cited by Applicant). Because the amino acid sequence of the human serotonin receptor that was described in Figure 14B (SEQ ID NO:8) of the Synaptic patent publication is greater than 94% identical to SEQ ID NO:2 of the instant application, it is encompassed by the limitations ""functional equivalent", "derivative", and encoded by a nucleic acid capable of hybridizing under conditions of high stringency.

11) Applicant is advised that a claim to "an isolated nucleic acid molecule encoding the amino acid sequence of SEQ ID NO:2" as well as a claim to "an isolated receptor protein comprising the amino acid sequence of SEQ ID NO:2" would be enabled and allowable over the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kunz Gary can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
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